

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule for assessing or modulating multidrug resistance (MDR) in a cell, said nucleic acid molecule encoding an Annexin family member.

2. The isolated nucleic acid molecule of claim 1, wherein said cell is selected from an animal cell, mammalian cell, a human cell, a parasitic cell and a fungal cell.

10

5

3. The isolated nucleic acid molecule of claim 1, comprising a nucleic acid sequence which is at least 90% identical to a sequence selected from the group consisting of a nucleotide sequence encoding an Annexin polypeptide selected from Annexin I to Annexin XI, or a nucleotide sequence complementary thereto.

15

4. The isolated nucleic acid molecule of claim 1, 2 or 3, wherein said Annexin is Annexin I and said Annexin polypeptide is the Annexin I polypeptide which comprises the complete amino acid sequence set forth in SEQ ID NO:2.

20

5. The isolated nucleic acid molecule of claim 1 or 2, wherein said Annexin is Annexin I and said nucleotide sequence comprises the nucleotide sequence as set forth in SEQ ID NO: 1.

25

6. A method of detecting and/or assessing an Annexin-based MDR phenotype in a sample comprising:

5

10

15

20

25

- a) contacting said sample with an isolated nucleic acid molecule consisting of 10 to 50 nucleotides specifically hybridizing to RNA and/or DNA encoding an Annexin, wherein said nucleic acid molecule is or is complementary to a nucleotide sequence consisting of at least 10 consecutive nucleotides from the nucleic acid sequence of one of Annexin I to XI, under hybridization conditions; and
- b) detecting the presence of said molecule bound to Annexin nucleic acid,
 wherein said presence of said Annexin nucleic acid correlates with an Annexinbased MDR in said sample.
 - 7. The method of claim 6, wherein said Annexin-based MDR is an Annexin I-based MDR.
- MDR phenotype in a sample, comprising at least one container means having disposed therein an isolated nucleic acid molecule consisting of 10 to 50 nucleotides specifically hybridizing to RNA and/or DNA encoding an Annexin, wherein said nucleic acid molecule is or is complementary to a nucleotide sequence consisting of at least 10 consecutive nucleotides from the nucleic acid sequence of one of Annexin I to XI; and wherein said presence and/or said quantification of Annexin nucleic acid sequence correlates with an Annexin-based MDR in said sample.
 - 9. The kit of claim 8, wherein said nucleotides specifically hybridize to Annexin I, thereby detecting and/or quantifying an Annexin I-based MDR.

10. A recombinant vector for modulating and/or increasing Annexin-based MDR in a cell comprising the isolated nucleic acid molecule of claim 1 operably linked to a promoter element.

Annexin I.

12. The recombinant vector of claim 11, being pCDNA3/P-40 or pC1N4P-40.

The recombinant vector of claim 10, wherein Annexin is

10

5

13. A cell that contains the recombinant vector of claim 10, 11 or 12; said cell having been rendered multidrug resistant (MDR) by said expression of said Annexin nucleic acid molecule.

15

14. The cell of claim 13, having been rendered MDR by the expression of recombinant Annexin I.

20 A

15. A method of identifying compounds that affect annexin-based MDR in a cell, said method comprising:

a) incubating said cell in the presence of a potential Annexin-based MDR-affecting compound in the presence and absence of a drug; and

b) assessing the effect of said compound on the resistance of said cell to said diug.

25

16. The method of claim 14, wherein said cell is a cell in accordance with one of claims 13 or 14.



17. The method of claim 15 or 16, wherein said compound is selected from the group consisting of a nucleic acid molecule encoding an Annexin variant, or a part thereof, a dominant negative mutant of an Annexin, a mutant Annexin, an antibody to Annexin, a peptide, and a small molecule.

18. The method of claim 17, wherein said compound is an Annexin I antisense molecule.

19. The method of one of claims 15, 16, 17 or 18, wherein said drug is an anticancer drug.

20. A method of reducing Annexin-based MDR in a cell comprising: administering thereto a the apeutically effective amount of a compound selected from the group consisting of a nucleic acid molecule, a dominant negative mutant of an Annexin, a mutant Annexin protein, an antibody to Annexin, a peptide, and a small molecule.

21. The method of claim 20, wherein said Annexin-based MDR is Annexin I-based.

22. The method of claim 21, wherein said compound is an Annexin I antisense molecule.

23. The method of claim 21, wherein said compound is a calcium chelator or a calcium channel blocker.

20

10

15

25

- 24. A pharmaceutical composition for reducing MDR in a cell comprising an Annexin-based MDR affecting compound together with a pharmaceutically acceptable carrier.
- 5 25. The pharmaceutical composition of claim 24, wherein said Annexin-based MDR is Annexin I-based, and said compound is an Annexin I-based MDR affecting compound.
- 26. A method of diagnosing the presence or predisposition of Annexin-based MDR in a patient comprising:

13

15

- a) taking a sample from said patient;
- b) determining the amount of Annexin protein and/or nucleic acid in said sample;
- c) diagnosing the presence or predisposition of Annexin-based MDR in said patient, wherein an increased amount of said Annexin protein and/or nucleic acid in said sample as compared to a control sample indicates the presence or predisposition towards Annexin-based MDR.
- 27. The method of claim 26, wherein said Annexin-based
 MDR is Annexin I-based and said determining is a determination of Annexin
 I protein and/or nucleic acid.
 - 28. A method of diagnosing the presence or predisposition of Annexin-based MDR in a pathogen comprising:
- 25 a) taking a sample from said pathogen;
 - b) determining the amount of Annexin protein and/or nucleic acid in said sample;

5

c) diagnosing the presence or predisposition of Annexin-based MDR in said pathogen, wherein an increased amount of said Annexin protein and/or nucleic acid in said sample as compared to a control sample indicates the presence or predisposition towards Annexin-based MDR.

29. The method of claim 28, wherein said Annexin-based MDR is Annexin I-based and said determining is a determination of Annexin I protein and/or nucleic acid.

add \

add)